Package leaflet: Information for the user

Irinotecan 20 mg/ml concentrate for solution for infusion

irinotecan hydrochloride trihydrate

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Irinotecan is and what it is used for

Irinotecan is an anticancer medicine containing the active substance irinotecan hydrochloride trihydrate.

Irinotecan hydrochloride trihydrate interferes with the growth and spread of cancer cells in the body.

Irinotecan is indicated in combination with other medicines for the treatment of patients with advanced or metastatic cancer of the colon or rectum.

Irinotecan may be used alone in patients with metastatic cancer of the colon or rectum whose disease has recurred or progressed following initial fluorouracil-based therapy.

2. What you need to know before you use Irinotecan

Do not use Irinotecan
- if you have chronic inflammatory bowel disease and/or bowel obstruction
- if you are allergic to irinotecan hydrochloride trihydrate or any of the other ingredients of this medicine (listed in section 6 “What Irinotecan contains”)
- if you are a breast-feeding woman (see section 2)
- if your bilirubin level is higher than 3 times the upper limit of the normal range
- if you have severe bone marrow failure
- if you are in poor general condition (WHO performance status higher than 2)
- if you are taking or have recently taken St John´s Wort (an herbal extract containing Hypericum)
- if you are to take or have recently taken live attenuated vaccines (vaccines against yellow fever, chicken pox, shingles, measles, mumps, rubella, tuberculosis, rotavirus, influenza) and during the 6 months after stopping chemotherapy

If you receive Irinotecan in combination with other medicines, please make sure that you also read the package leaflet of the other medicines regarding additional contraindications.

Warnings and precautions:
Talk to your doctor, pharmacist or nurse before using Irinotecan

Take special care with Irinotecan. The use of Irinotecan should be confined to units specialised in the administration of cytotoxic chemotherapy and it should only be administered under the supervision of a physician qualified in the use of anticancer chemotherapy.

If you have Gilbert's syndrome, an inherited condition that can cause elevated bilirubin levels and jaundice (yellow skin and eyes)

Diarrhoea
Irinotecan can cause diarrhoea, which in some cases may be severe. This may start a few hours or a couple of days after the medicine infusion. If left untreated, it could lead to dehydration and serious chemical imbalances, which can be life threatening. Your doctor will prescribe medicine to help prevent or control this side effect. Make sure you get the medicine right away, so that you will have it at home when you need it.

- Take the medicine as prescribed at the first sign of loose or frequent bowel movements.
- Drink large amounts of water and (or) salty drinks (fizzy water, soda or soup).
- Call your doctor or nurse know if you still have diarrhoea, especially if it lasts more than 24 hours, or if you get lightheaded, dizzy, or faint.

Neutropenia (decrease in some white blood cells)
This medicine can lower your white blood cell count, mainly in the weeks after the medicine is given. This can increase the risk of getting an infection. Be sure to let your doctor or nurse know right away if you have any signs of infection, such as fever (38°C or higher), chills, pain when passing urine, a new cough, or bringing up sputum. Avoid being near people who are sick or have infections. Tell your doctor at once if you develop signs of infection.

Blood monitoring
Your doctor will likely test your blood before and during your treatment, to check for effects of the medicine on blood counts or on blood chemistry. Based on the test results, you may need medicines to help treat the effects. Your doctor may also need to reduce or delay your next dose of this medicine, or even stop it altogether. Keep all your appointments for doctor visits and lab tests.

This medicine may lower your platelet count in the weeks after it is given, which can increase your risk of bleeding. Speak with your doctor before taking any medicines or supplements that might affect your body's ability to stop bleeding, such as aspirin or aspirin-containing medicines, warfarin, or vitamin E. Tell your doctor right away if you have unusual bruising, or bleeding such as nosebleeds, bleeding gums when you brush your teeth, or black, tarry stools.

Nausea and vomiting
You may have nausea and vomiting on the day you receive this medicine or in the first few days after. Your doctor may give you medicine before your treatment to help prevent nausea and vomiting. Your doctor will likely prescribe anti-nausea medicines that you can take at home. Have these medicines on hand for when you need them. Call your doctor if you are unable to take fluids by mouth due to nausea and vomiting.

Acute cholinergic syndrome
This medicine may affect part of your nervous system that controls body secretions, leading to what is known as cholinergic syndrome. Symptoms can include runny nose, increased saliva, excess tears in the eyes, sweating, flushing, abdominal cramps, and diarrhoea. Let your doctor or nurse know right away if you notice any of these symptoms, as there are medicines that can help control them.

Lung disorders
Rarely, people on this medicine have serious lung problems. Tell your doctor right away if you have new or worsening cough, trouble breathing, and fever. Your doctor may need to stop your treatment to manage this problem.

This medicine may increase your risk of major blood clots in the veins of the legs or lungs, which can travel to other parts of the body such as the lungs or brain. Tell your doctor right away if you notice chest pain, shortness of breath, or swelling, pain, redness, or warmth in an arm or leg.

Chronic intestinal inflammation and/or intestinal blockage
Call your doctor if you have pain in your belly and you cannot move your bowels, especially if you also have bloating and loss of appetite.

Irradiation therapy
If you recently received treatment with pelvic or abdominal radiotherapy, you may be at increased risk of developing bone marrow suppression. Please talk to your doctor before starting the Irinotecan.

Kidney function
Occurrences of kidney dysfunction have been reported.

Cardiac disorders
Inform your doctor if you suffer/suffered from heart disease or if you previously received anticancer medicines. Your doctor will monitor you closely and discuss with you how risk factors (for example smoking, high blood pressure and to high fat content) can be reduced.

Vascular disorders
Irinotecan is rarely associated with blood flow disorders (blood clots in the vessels of your legs and lungs) and it may occur rarely in patients with multiple risks factors.

Others
This medicine may cause sores in the mouth or on the lips, often within the first few weeks after starting treatment. This can cause mouth pain, bleeding, or even trouble eating. Your doctor or nurse can suggest ways to reduce this, such as changing the way you eat or how you brush your teeth. If needed, your doctor can prescribe medicine to help with the pain.

Tell your doctor or dentist that you are on this medicine if you are planning to have surgery or any procedure.

If used in combination with other anticancer medicines for your condition please make sure that you also read the leaflets for the other medicine.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Other medicines and Irinotecan

Irinotecan can interact with a number of medicines and supplements, which may either raise or lower the level of the medicine in your blood. Tell your doctor or pharmacist if you are using, have recently used or might use any of the following:

- Medicines used to treat seizure (carbamazepine, phenobarbital, phenytoin and
- fosphenytoin)
- Medicines used to treat fungal infection (ketoconazole, itraconazole, voriconazole and
- posaconazole)
- Medicines used to treat bacterial infection (clarithromycine, erythromycin and telithromycine)

- Medicines used to treat tuberculosis (rifampicin and rifabutin)
- St John's Wort (a herbal dietary supplement)
- Live attenuated vaccines
- Medicines used to treat HIV (indinavir, ritonavir, amprenavir, fosamprenavir, nelfinavir,
- atazanavir, and others)
- Medicines used to suppress your body's immune system to prevent transplant rejection (cyclosporine and tacrolimus)
- Medicines used to treat cancer (regorafenib, crizotinib, idelalisib and apalutamide)
- Vitamin K antagonists (common blood thinner such as Warfarin)
- Medicines used to relax muscles used during general anaesthesia and surgery (suxamethonium)
- 5-fluorouracil/folinic acid
- Bevacizumab (a blood vessel growth inhibitor)
- Cetuximab (an EGF receptor inhibitor)

Tell your doctor pharmacist or nurse before being given irinotecan if you are already having, or have recently had chemotherapy (and radiotherapy).

Don't start or stop taking any medicines while you are on Irinotecan without talking with your doctor first.

This medicine can cause serious diarrhoea. Try to avoid laxatives and stool softeners while taking this medicine.

There may be more medicines that interact with Irinotecan. Check with your doctor, pharmacist or nurse about your other medicines, herbs, and supplements, and whether alcohol can cause problems with this medicine.

Pregnancy, breast-feeding and fertility
Women of childbearing potential and men have to use effective contraception during and up to 1 month and 3 months after treatment respectively.

Pregnancy
This medicine may cause problems with the foetus if taken at the time of conception or during pregnancy. Men and women who are taking this medicine should use reliable birth control during treatment. It is important to check with your doctor about what kinds of birth control can be used with this medicine. In pregnant women, treatment with this medicine should be used only if the potential benefit to the mother outweighs the risk to the foetus.

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Breast-feeding
No studies have been done, nevertheless, this medicine may pass into breast milk and affect the baby. Breast-feeding should be discontinued for the duration of your treatment with this medicine.

If you are breast-feeding ask your doctor or pharmacist for advice before taking this medicine.

Fertility
No studies have been done, nevertheless, this medicine may affect fertility. Talk with your doctor about the possible risk with this medicine and the options that may preserve your ability to have children.

Driving and using machines

You may notice that you are dizzy and/or have trouble with your vision in the first 24 hours or so after you take this medicine. Do not drive or operate machinery if you have this side effect.

Irinotecan contains sorbitol and sodium

This medicine contains 45 mg sorbitol in each ml of concentrate. Sorbitol is a source of fructose. If you (or your child) have hereditary fructose intolerance (HFI), a rare genetic disorder, you (or your child) must not receive this medicine. Patients with HFI cannot break down fructose, which may cause serious side effects.

You must tell your doctor before receiving this medicine if you (or your child) have HFI or if your child can no longer take sweet foods or drinks because they feel sick, vomit or get unpleasant effects such as bloating, stomach cramps or diarrhoea.

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Irinotecan

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Irinotecan will be given to you by healthcare professionals.

Your doctor may recommend a DNA test before your first dose of Irinotecan.

Some people are genetically more likely to have certain side effects from the medicine.

The amount of Irinotecan that you will receive depends on many factors, including your height and weight, your general health or other health problems, and the type of cancer or condition being treated. Your doctor will determine your dose and schedule.

Irinotecan is injected into a vein through an intravenous route (IV). You will receive this injection in a clinic or hospital setting. Irinotecan must be given slowly, and the IV infusion can take up to 90 minutes to complete.

You may be given other medications to prevent nausea, vomiting, diarrhoea, and other side effects while you are receiving Irinotecan. You may need to keep using these medicines for at least a day after your Irinotecan injection.

Tell your care givers if you feel any burning, pain, or swelling around the IV needle when Irinotecan is injected. If the medicine escapes from the vein it can cause tissue damage. If you experience pain or notice redness or swelling at the IV site while you are receiving Irinotecan, alert your healthcare professional immediately.

There are currently several treatment schedules recommended for Irinotecan. It is usually given either once every 3 weeks (Irinotecan given alone) or once every 2 weeks (Irinotecan given in combination with 5FU//FA chemotherapy). The dose will depend on a number of factors, including the treatment schedule, your body size, your age and general health, your blood counts, how well your liver is working, whether you have had radiation to your abdomen/pelvis, and whether you have any side effects such as diarrhoea.

Only your doctor may assess the duration of treatment.

If you use more Irinotecan than you should:
Seek emergency medical attention. Overdose symptoms may include some of the serious side effects listed in this medication guide.
If you forget to use Irinotecan
Call your doctor for instructions if you miss an appointment for your Irinotecan injection.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Some side effect could be serious. You must immediately contact your doctor if you experience any of those following serious side effects (see section 2).

Get emergency medical help if you have any of these signs of an allergic reaction: hives; difficult breathing; swelling of your face, lips, tongue, or throat.

- diarrhoea (see section 2).
- Early diarrhoea: Occurring within 24 hours of receiving this medicine, accompanied by symptoms runny nose, increased salivation, watery eyes, sweating, flushing, abdominal cramping. (This can occur while the medicine is being administered. If so, alert your healthcare professional promptly. Medication can be given to stop and/or lessen this early side effect).
- Late diarrhoea: Occurring greater than 24 hours of receiving this medicine. Because of concerns of dehydration and electrolyte imbalances with diarrhoea it is important to be in contact with health care professionals for monitoring, and for medication and diet modifications advice.

Talk to your doctor or nurse if you experience any of the symptoms below

Symptoms	Frequency* of occurrence in Monotherapy	Frequency† of occurrence in Combination Therapy
Abnormally low number of white blood cells which could put you at increased risk for infection	Very common	Very common
Low number of red blood cells causing tiredness and shortness of breath	Very common	Very common
Decreased appetite	Very common	Very common
Cholinergic syndrome (see Take special care with Irinotecan)	Very common	Very common
Vomiting	Very common	Very common
Nausea	Very common	Very common
Abdominal pain	Very common	Common
Hair loss (reversible)	Very common	Very common
Inflammation of mucous membranes	Very common	Very common
Fever	Very common	Common

Feeling weak and having no energy	Very common	Very common
Low number of platelets (blood cells that help with clotting) which may cause bruising or bleeding	Common	Very common
Abnormal liver function test values	Common	Very common
Infection	Common	Common
Low number of white blood cells with fever	Common	Common
Difficulty in passing stools	Common	Common
Abnormal kidney function test values	Common	Not reported

* Very common: may affect more than 1 in 10 people

† Common: may affect up to 1 in 10 people

Not known: frequency cannot be estimated from the available data

- Severe, persistent or bloody diarrhoea (which may be associated with stomach pain or fever) caused by bacteria called (Clostridium difficile)
- Blood infection
- Dehydration (due to diarrhoea and vomiting)
- Dizziness, rapid heartbeat and pale skin (a condition called hypovolaemia)
- Allergic reaction
- Temporary speech disorders during or shortly after treatment
- Pins and needles
- High blood pressure (during or after infusion)
- Heart problems*
- Lung disease causing wheezing and shortness of breath (see section 2)
- Hiccups
- Intestinal blockage
- Enlarged colon
- Bleeding from the bowels
- Inflammation of the large intestine
- Abnormal lab test results
- Hole in the intestine
- Fatty liver disease
- Skin reactions
- Reactions at the site where the medicine was administered
- Low level of potassium in the blood
- Low level of salt in the blood mostly related with diarrhoea and vomiting
- Muscle cramps
- Kidney problems*
- Low blood pressure*
- Fungal infections
- Viral infections

* Infrequent cases of these events have been observed in patients who experienced episodes of dehydration associated with diarrhoea and/or vomiting, or infections of the blood.

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

For the UK:
Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App store.

For Ireland:
HPRA Pharmacovigilance
Website: www.hpra.ie

5. How to store Irinotecan

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and labels after EXP. The expiry date refers to the last day of that month.

Store below 25°C. Keep vial in the outer carton in order to protect from light. Do not freeze.

After dilution:
Chemical and physical in-use stability has been demonstrated for 24 hours below 25°C and for 48 hours at 2°C to 8°C.

From a microbiological point of view, the product should be used immediately after first opening. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C unless the dilution has taken place in controlled and validated aseptic conditions.

Do not use this medicine if you notice particles visible in the concentrate or infusion solution.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Irinotecan contains
- The active substance is Irinotecan hydrochloride trihydrate. Each ml contains 20 mg Irinotecan hydrochloride trihydrate, equivalent to 17.33 mg Irinotecan.
  Each vial with 2 ml contains 40 mg Irinotecan hydrochloride trihydrate.
  Each vial with 5 ml contains 100 mg Irinotecan hydrochloride trihydrate.
  Each vial with 15 ml contains 300 mg Irinotecan hydrochloride trihydrate.
  Each vial with 25 ml contains 500 mg Irinotecan hydrochloride trihydrate.
- The other ingredients are sorbitol (E420), lactic acid, water for injections and sodium hydroxide (used to adjust pH).

What Irinotecan looks like and contents of the pack

Irinotecan 20 mg/ml concentrate for solution for infusion is light yellow colored solution and free from visible particles, packed in glass vials.

The product is available as single vials containing either 40 mg/2 ml, 100 mg/5 ml, 300 mg/15 ml or 500 mg/25 ml. These vials are for single use only.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

For UK:
Fresenius Kabi Limited
Cestrian Court
Eastgate Way, Manor Park
Runcorn, Cheshire, WA7 1NT
United Kingdom

For Ireland:
Fresenius Kabi Deutschland GmbH
Else-Kröner-Straße 1,
61352 Bad Homburg v.d.Höhe
Germany

Manufacturer
Fresenius Kabi Deutschland GmbH
Pfingstweide 53
61169 Friedberg
Germany

This medicinal product is authorised in the Member States of the EEA under the following names:

Czech Republic	Irinotecan Kabi
Denmark	Irinotecan Fresenius Kabi
Estonia	Irinotecan Kabi 20 mg/ml
Finland	Irinotecan Fresenius Kabi 20 mg/ml infuusiokonsentraatti, liuosta varten
Hungary	Irinotecan Kabi 20 mg/ml koncentrátum oldatos infúzióhoz
Ireland	Irinotecan 20 mg/ml concentrate for solution for infusion
Italy	Irinotecan Kabi
Latvia	Irinotecan Kabi 20 mg/ml koncentrāts infūziju šķīduma pagatavošanai
Lithuania	Irinotecan Kabi 20 mg/ml koncentratas infuziniam tirpalui
Poland	Irinotecan Kabi
Slovak Republic	Irinotecan Kabi 20 mg/ml infúzny koncentrát
Spain	Irinotecán Kabi 20 mg/ml concentrado para solución para perfusión EFG
United Kingdom (NI)	Irinotecan 20 mg/ml concentrate for solution for infusion

This leaflet was last revised in December 2021.

The following information is intended for healthcare professionals only:

Instruction for use

Cytotoxic

Handling of Irinotecan

As with all antineoplastic agents, caution should be exercised when handling Irinotecan. Dilution should be carried out under aseptic conditions by trained personnel in a designated area. Precautions should be taken to avoid contact with the skin and mucous membranes.

Protection instructions for preparation of Irinotecan solution for infusion

1. Protective chamber should be used and protective gloves as well as protective gown should be worn. If there is no protective chamber available mouth cover and goggles should be used.
2. Opened containers, like injection vials and infusion bottles and used cannulae, syringes, catheters, tubes, and residuals of cytostatics should be considered as hazardous waste and undergo disposal according to local guidelines for the handling of HAZARDOUS WASTE.
3. Follow the instructions below in case of spillage:
    - protective clothing should be worn
    - broken glass should be collected and placed in the container for HAZARDOUS WASTE
    - contaminated surfaces should be flushed properly with copious amounts of cold water
    - the flushed surfaces should then be wiped thoroughly and the materials used for wiping should be disposed as HAZARDOUS WASTE
4. In the event of Irinotecan contact with the skin, the area should be rinsed with plenty of running water and then washed with soap and water. In case of contact with mucous membranes, wash the contacted area thoroughly with water. If you have any discomfort, contact a doctor.
5. In case of contact of Irinotecan with eyes, wash them thoroughly with plenty of water. Contact an ophthalmologist immediately.

Preparation of infusion solution

Irinotecan concentrate for solution for infusion is intended for intravenous infusion only after diluting prior to administration in the recommended diluents, either 0.9 % Sodium chloride solution for infusion or 5% glucose solution for infusion. Aseptically withdraw the required amount of Irinotecan concentrate for solution from the vial with a calibrated syringe and inject into a 250 ml infusion bag or bottle. The infusion should be thoroughly mixed by manual rotation.

The final solution is clear, colourless to light yellow in colour and free from visible particles.

If any precipitate is observed in the vials or after dilution, the product should be discarded according to standard procedures for cytotoxic agents.

Read the package leaflet for the shelf life of the diluted product.

Irinotecan should **not** be delivered as an intravenous bolus or an intravenous infusion shorter than 30 minutes or longer than 90 minutes.

Disposal

All items used for preparation, administration or otherwise coming into contact with irinotecan should undergo disposal according to local guidelines for the handling of cytotoxic compounds.